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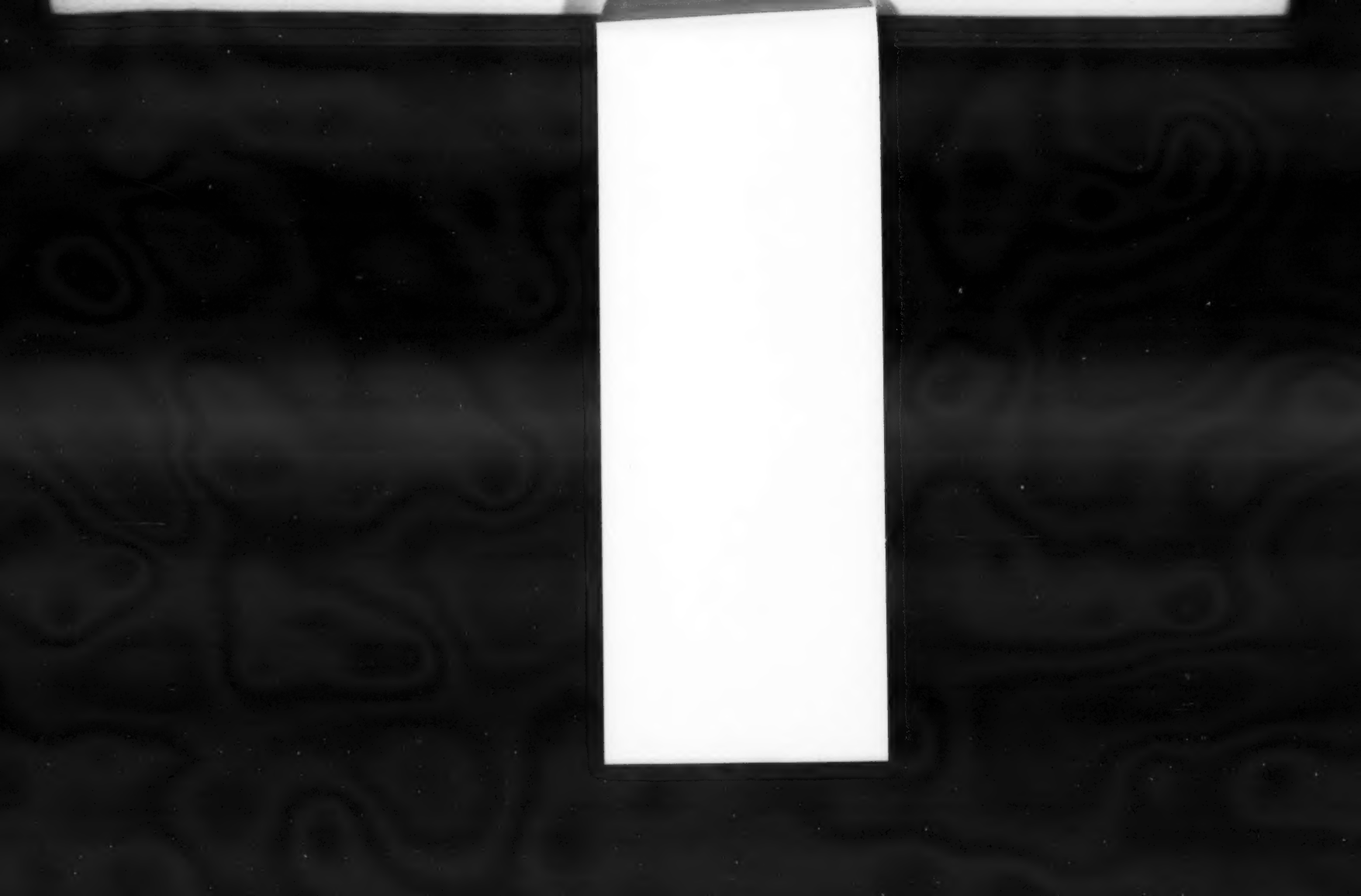
CORRECTION.

On page 13 of the January 1928 issue lead III in Figure 3 was erroneously exchanged with lead III in Figure 5, page 15.



THE INACTIVATION OF THE CHICKEN-TUMOR VIRUS BY MEANS OF CALCIUM COMPOUNDS[1,2]

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In an earlier investigation upon the adsorption of certain viruses by means of particulate matter (1927 b), it was found that precipitated chalk inactivated the chicken-tumor virus. This result, together with the fact that lime is sometimes used in the manufacture of carmine powder, which inactivates the tumor virus (1927 a), led to the investigation of the effect of a few of the calcium compounds upon the same virus.

The calcium compounds tested were calcium oxide, carbonate, chloride, lactate, sulphate, phosphate, and plaster of Paris. Of these the oxide was the most potent in bringing about the inactivation of the chicken-tumor virus.

The tumor used and the method employed were the same as those described in previous publications (1927 a, b, c), except that 5 cc. instead of 2 cc. of the tumor extract were added to the desired amount of the calcium compound. This was centrifuged and the supernatant fluid and the washed deposit used for injection. Certain of the calcium salts became dissolved in the tumor extract so that they were tested as solutions. In some instances the tumor extracts containing calcium oxide, calcium carbonate and plaster of Paris, were not centrifuged but were injected as suspensions.

CALCIUM OXIDE

This calcium compound was added to the tumor extract in amounts equivalent to 2.5, 1, and 0.5 per cent. These experiments were repeated as many as five times, and in every instance the injection of the supernatant fluid and of the washed deposit as well as of the uncen-

[1] Received for publication June 30, 1927.
[2] Aided by a grant from the Bache fund.

trifuged suspension failed to bring about the growth of a tumor, whereas the injection of the tumor extract without the calcium oxide was followed by a malignant growth.

CALCIUM CARBONATE

This salt was used in amounts equivalent to 25, 2, 1, 0.5, and 0.4 per cent and was tested with the extracts of seven tumors. When as much as 25 per cent of precipitated chalk was added to the tumor extract both the supernatant fluid and the washed deposit failed to produce a tumor. The addition of small amounts of chalk to the tumor extract sometimes prevented and sometimes did not prevent the growth of a tumor. The result varied with the different tumors from which the extract was made rather than with the amount of the carbonate used. In one instance, when as much as 100 mgm. of the chalk were added to 5 cc. of the tumor extract, both the supernatant fluid and the washed deposit, when injected into the breast of a chicken, brought about the growth of a tumor, while in another instance, when only 50 mgm. of the carbonate were added to the same amount of extract of another tumor, neither the supernatant fluid nor the washed deposit produced a tumor. The same was true when the mixture of tumor extract and carbonate was not centrifuged but was injected as a suspension, for in experiments in which extracts from three tumors were used, injection of the suspensions from two of them, each containing one per cent of chalk, resulted in a tumor, while that from a third containing the same amount of chalk did not. When these experiments were repeated, 0.5 per cent of chalk instead of 1 per cent being employed, the extracts from two other tumors were not inactivated while that from a third was. On the whole, then, chalk sometimes inactivated the tumor virus but more frequently failed to do so. These conflicting results are interesting in view of the fact that in many of the investigations the same tumor extracts were used for the experiments with the carbonate as were used for those with the oxide which invariably gave negative results.

CALCIUM LACTATE

This salt was soluble in the tumor extract. Only three amounts of it were tested and the experiments were performed only once. One

chicken received 5 cc. of tumor extract containing 1.6 per cent of the lactate in the breast muscle. This produced a slight induration at the site of the inoculation. The swelling disappeared and the chicken failed to develop a tumor. It was autopsied at the end of a month and the muscle was found to be normal with no sign of tumor. One chicken was used to test the other two amounts. It received 5 cc. of another tumor extract containing 1.5 per cent of calcium lactate in one side of the breast and the same amount of extract containing 0.75 per cent of the salt in the other. These amounts of calcium lactate did not inactivate the tumor virus and the chicken developed a large tumor in each side of the breast.

CALCIUM SULPHATE

This compound was tested only once. In this experiment 50 mgm. of the calcium sulphate were added to 5 cc. of a tumor extract, shaken and centrifuged. The deposit, washed in the usual manner, was injected into the breast of a chicken where it caused the growth of a tumor. The supernatant fluid also brought about the growth of a tumor in the chicken into which it was injected.

CALCIUM CHLORIDE

Calcium chloride was added to tumor extracts in amounts of 10, 2, and 1 per cent. It became dissolved in the extract and was injected as a solution rather than as a suspension. It produced marked swellings at the sites of the injections. These did not disappear, but tumor tissue developed in and around them, showing that the calcium chloride had not inactivated the virus.

CALCIUM PHOSPHATE

Five different kinds of calcium phosphate were tested. These were the mono-basic, di-basic, tri-basic, hexose, and glycero-phosphate. The mono-basic phosphate was tried with extracts of four tumors. It was soluble in the extract and formed an acid solution. It was added to the extracts in amounts proper to form 2.5, 1.6, 1.5, 1, 0.75 per cent solutions, respectively. Each of these failed to produce a tumor when injected into the breast of a chicken. The other phosphates were tested

only once and only by the addition of 50 milligrams (1 per cent) of the compound to the 5 cc. of the extract. All of these except the hexose-phosphate failed to inactivate the virus and growth of a tumor resulted.

PLASTER OF PARIS

In order to compare our results with those of Kramer (1927) on bacterial filters, commercial plaster of Paris was added to the tumor extract in concentrations of 2, 1 and 0.5 per cent. Extracts of three tumors were used. In the experiments in which 2 per cent of plaster of Paris was added to the tumor extracts both the supernatant fluids and the washed deposits failed to bring about the growth of a tumor when injected into the breast of a chicken. The addition of less plaster of Paris (1 and 0.5 per cent) did not inactivate the virus, and the injection of the suspensions of the tumor extract containing these amounts of plaster of Paris as well as of the supernatant fluids and of the washed deposits from such suspensions produced a tumor in the breasts of the chickens.

DISCUSSION

There is an extensive literature on the adsorption of toxins, antitoxins, lysins, antilysins, enzymes, viruses and drugs by means of various substances. These investigations were largely inspired by the observations of Metchnikoff and his contemporaries on phagocytosis. Several of the many investigators in this field used some of the calcium compounds as adsorbents. Roux and Yersin (1889) found that calcium phosphate partly adsorbed diphtheria toxin; Vaillard and Vincent (1890) stated that phosphate of calcium adsorbed part of the tetanus toxin but did not hold it in the animal; and Levaditi and Nicolau (1923) stated that calcium tri-phosphate adsorbed totally the vaccine virus. It is difficult to draw any conclusions as to whether the calcium compounds adsorbed the chicken-tumor virus, since in no instance did any amount of any calcium compound tried render the supernatant fluid inactive without at the same time rendering the washed deposit inactive, and when the deposit was active the supernatant fluid was also active. Any amount of any of the calcium compounds that rendered the supernatant fluid and washed deposit in-

active also inactivated the uncentrifuged suspension. There is, of course, a probability that the inactivation of the tumor virus by means of certain of the calcium compounds was due to a chemical change rather than to its adsorption by the particulate matter. Nevertheless, where the calcium compound which was added to the tumor extract took up so much of the tumor virus that, although the deposit was well washed, it was still able to bring about the growth of a tumor (as for instance the deposit from 1 per cent plaster of Paris or that from 1 per cent calcium sulphate), it seems as though this phenomenon might be interpreted as corresponding to the adsorption but not fixation of the virus by the calcium particles. Although calcium carbonate always inactivated the virus when added to the tumor extract in large amounts, when small amounts were added, it frequently failed to do so, and it became possible for the washed deposit from even as little as 0.4 per cent of calcium carbonate to bring about the growth of a tumor. From this it seems as though the chalk may be said to have adsorbed the virus.

In discussing the results of experiments such as ours, it is necessary to remember that the virus may be changed by the acidity, alkalinity, or salt content of the solution in which it is tested; also, that any change in these properties of the solution may change the phenomenon of adsorption taking place between the substances in the solution. It is interesting in this connection to note that the chicken-tumor virus was inactivated by calcium oxide, which forms an alkaline solution, and also by calcium mono-basic phosphate, which forms an acid solution.

Kramer (1927) found that plaster of Paris filters removed certain substances which passed the Berkefeld filter. From this he concluded that the substances that passed the negatively charged diatomaceous earth but not the plaster of Paris had a negative charge. He also stated that filters made of pure calcium sulphate did not behave in this way and that the efficiency of the commercial plaster of Paris filter was due to a trace of calcium carbonate. He claimed that the addition of calcium carbonate to the calcium-sulphate filters renders them more capable of holding back the acid or negatively charged substances and that the addition of 25 per cent of magnesium oxide calcined at 1300°C. made the Berkefeld filter more efficient in retaining the basic or positively charged substances.

It is hardly possible to decide whether the chicken-tumor virus is positively or negatively charged, although from our results it seems more probable that it is negative rather than positive, since we have found that it is inactivated by as little as 2 per cent of plaster of Paris, by 2 per cent of iron oxide and by certain aluminium salts, but is not inactivated, although it is partly adsorbed, by 50 per cent of kaolin or by 50 per cent of powdered Berkefeld filter.

In this connection it may be of interest to quote briefly the results of our present as well as of our previous investigations: The tumor virus was

Partly adsorbed but not fixed by:
- 50.0 per cent Berkefeld filter
- 50.0 per cent Kaolin
- 50.0 per cent Animal charcoal
- 50.0 per cent Vegetable charcoal
- 25.0 per cent Cuttlebone
- 1.0 per cent Magnesium oxide, calcined
- 1.0 per cent Calcium sulphate

i.e., both the supernatant fluid and the washed deposit produced a tumor.

Not inactivated by as much as:
- 50.0 per cent India ink
- 10.0 per cent Calcium chloride
- 1.0 per cent Trypan blue
- 1.0 per cent Di-basic calcium phosphate
- 1.0 per cent Tri-basic calcium phosphate
- 1.0 per cent Calcium glycero-phosphate
- 0.5 per cent Glue
- Carmine solutions (saturated)
- Sodium hydroxide (pH 10)
- Hydrochloric acid (pH 4)
- Plasma *in vivo*
- White blood cells *in vivo*

i.e., tumor extracts containing this amount of these substances produced tumors.

Adsorbed but not fixed by:
- 10.0 per cent Aluminium hydroxide
- 10.0 per cent Manganese dioxide

i.e., the supernatant fluid did not produce a tumor while the washed deposit did.

Was inactivated by:
- 0.5 per cent Calcium oxide
- 0.75 per cent Calcium mono-basic phosphate
- 1.0 per cent Aluminium lactate

1.0 per cent Aluminium mono-hydrate
1.0 per cent Calcium carbonate (sometimes)
1.0 per cent Calcium hexose-phosphate
2.0 per cent Plaster of Paris
2.0 per cent Iron oxide
2.5 per cent Carmine powder
2.5 per cent Aluminium chloride
10.0 per cent Aluminium sulphate

Adsorbed and inactivated by:
2.0 per cent Plaster of Paris
2.5 per cent Carmine powder
25.0 per cent Calcium carbonate
37.0 per cent Aluminium hydroxide

i.e., both the supernatant fluid and the washed deposit failed to produce a tumor, while when smaller amounts of the same substance were used the washed deposit did produce a tumor, showing that in the latter instance the substance had adsorbed part of the virus but had not fixed it.

CONCLUSION

The addition of calcium oxide, calcium mono-basic phosphate and calcium hexose phosphate in as small amounts as 0.5, 0.75, and 1 per cent, respectively, to the chicken-tumor extract (1 to 10) inactivated the virus and prevented the growth of a tumor. The addition of large amounts (25 per cent) of calcium carbonate to the tumor extract adsorbed and fixed the virus. Small amounts (1 per cent) sometimes inactivated the virus but more frequently, although the virus was partly adsorbed, it was not fixed by this amount of calcium carbonate. The addition of 2 per cent of plaster of Paris to the tumor extract inactivated the virus, but when only 1 per cent of plaster of Paris was added to the extract, both the supernatant fluid and the washed deposit caused the growth of a tumor when injected into the breast of a chicken.

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THE PURIFICATION OF HEPARIN AND ITS CHEMICAL AND PHYSIOLOGICAL REACTIONS[1]

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An anticoagulant obtained from the dog's liver was described by Howell and Holt in 1918 (1). This substance was prepared from an ethereal extract of liver dried at a temperature of 60° to 80°F., and was designated provisionally as heparin. Owing to the method of preparation and its content in phosphorus it was assumed, erroneously, to belong to the group of phosphatids. The anticoagulant action of this material, although distinct, was not very strong, 1 milligram being required to prevent the coagulation of 1 to 2 cc. of blood. Since the product obtained proved to be soluble in water and insoluble in alcohol and ether, Howell in 1922 (2) devised a different method of preparation, starting with an aqueous or saline extract of the dried liver. The material obtained by this method exhibited a much stronger anticoagulant action, 1 milligram being sufficient to prevent clotting of 5 cc. of blood. Intravenous injections of its solution caused no toxic reactions and when used in proper concentrations made the blood of the animal entirely incoagulable for a certain period. Since the potency of this preparation was of the same order as that of hirudin, and since the latter material was difficult to procure, the firm of Hynson, Westcott and Dunning, of Baltimore, undertook to prepare heparin commercially for the use of laboratory workers desiring a suitable anticoagulant for experimental purposes. The method used in its preparation did not yield a constant product, although the material could be standardized to a definite potency. It was evident, however, that the active element was mixed with more or less inactive material, and repeated efforts have been made to isolate the substance in at least an approximate state of purity in order to determine its probable chemical nature. Numerous procedures used for

[1] Received for publication January 19, 1928.

this purpose (3) were successful in increasing the potency of the preparation. Products were obtained in which 1 mgm. sufficed to prevent clotting of 20 or even 40 cc. of blood and which gave no reaction for phosphorus. This last result demonstrated that the active substance is not a phosphatid as was supposed at first. Lately a method has been devised which gives the substance in apparently pure form, in a form at least which shows constant reactions and which is free from both nitrogen and phosphorus. The anticoagulant action for human blood is of the order of 1 mgm. to 100 cc. of blood.

METHOD

The method consists essentially of two procedures. First, adsorption of impurities by Lloyd's reagent in acid solution, and second, precipitation of the active substance by barium hydroxide. Repeated treatment with the Lloyd's reagent alone in 4 per cent acetic acid gives a preparation that is very active so that 1 mgm. will prevent the clotting of 50 cc. of human blood. The further purification by barium precipitation is attended by considerable loss of material, but yields a purer and more active substance. The details are as follows. Crude heparin prepared by the method of 1922 (2) was dissolved in water, 1 gram of heparin to 50 cc. of water, and digested for 6 to 12 hours at body temperature with taka-diastase to hydrolyze any glycogen that might be present. The solution was then filtered, evaporated on a water-bath nearly to dryness and boiled with a large volume of 95 per cent methyl alcohol for an hour, a reflux condenser being employed. The alcohol was removed by filtration and evaporation, the solid residue was dissolved in 1 per cent solution of sodium chloride, filtered and precipitated by the addition of an equal volume of acetone. This precipitate was collected by centrifugalizing, washed with 50 per cent acetone, dissolved in water, and treated with Lloyd's reagent in acid solution. Three successive treatments were used with this reagent in 2, 4, and 8 per cent acetic acid. After each treatment the solution was filtered first through a Buchner filter and then through filter paper. The final solution was neutralized with dilute sodium hydroxide and precipitated by the addition of an equal volume of acetone. The precipitate was collected by centrifugalizing, washed, dried, dissolved in water and filtered. This solution was then treated

with an excess of a saturated solution of barium hydroxide. The white precipitate was centrifugalized off, washed with water by layering in the centrifugal tube, and then stirred up with water and dilute hydrochloric acid added to distinct acid reaction. This mixture was centrifugalized and the clear supernatant liquid was poured off. The barium in this solution was precipitated by very careful addition of sodium sulphate or sulphuric acid, avoiding an excess. The barium precipitate was centrifugalized off, the supernatant liquid was neutralized with dilute sodium hydroxide and then after filtration evaporated to dryness on a water-bath. The residue obtained was treated with water. If it did not all dissolve the solution was filtered, evaporated to dryness and dissolved in water. This treatment was repeated until the residue obtained on evaporation dissolved completely in water. The final solution was precipitated by the addition of an equal volume of acetone. To ensure the separation out of a precipitate, sodium acetate was added to a concentration of one half per cent. The precipitate was centrifugalized off, washed with 50 per cent acetone and finally with acetone and ether. The material thus obtained is amorphous and readily soluble in water, although insoluble in all other solvents used. When its aqueous solutions are evaporated over the water-bath it is deposited in the form of a transparent glassy membrane. It was found that solutions of crude heparin and of the product obtained after treatment with the Lloyd's reagent give a blue color with the phenol reagent of Folin and Dennis, but after purification by barium precipitation the final product should give no trace of this reaction.

REACTIONS

Aqueous solutions of the purified heparin give the following reactions.

1. A negative test for phosphorus and nitrogen (sodium cyanide test).
2. It is not precipitated by salts of copper, zinc, cadmium, nickel, iron or platinum. It is precipitated by basic acetate of lead.
3. Barium hydroxide gives a white precipitate which turns canary yellow on boiling.
4. It gives the alpha naphthol reaction for carbohydrates.
5. Treated with Fehling's solution it gives no reduction, but if

first hydrolyzed thoroughly with dilute acid (HCl), it reduces Fehling's solution readily.

6. It gives no color reaction with iodine.

7. It gives a positive reaction for glycuronic acid with naphthoresorcin. The test was made according to the directions given by Tollens. To the heparin solution was added an alcoholic solution of naphthoresorcin, 0.1 cc. for each cubic centimeter of solution, and then an equal volume of concentrated HCl. The mixture was boiled gently for a minute and then allowed to cool for 3 or 4 minutes. Addition of ether gave a red violet layer showing an absorption band at D. When benzol was used in place of ether, the coloration took place much more slowly. It should be stated, however, that when the "Absatz" method was used the alcoholic solution instead of showing a violet color was reddish with a green fluorescence by reflected light.

8. It gives a positive reaction for glycuronic acid with orcinol (Bial's reagent). Two cubic centimeters of the Bial's reagent (HCl 100 cc., orcinol 200 mgm., ferric chloride (liq. ferri sesquichl.) 4 drops) were boiled and the heparin solution added a drop at a time. A fine green color developed, as is the case with glycuronic acid and the pentoses. In aqueous solution or after extraction with amyl alcohol an absorption band was obtained between D and C. When orcinol was used without the iron (Salkowski's method) this color reaction was not obtained, but the same negative result followed when glycuronic acid, prepared from euxanthinic acid, was tested in the same way. Although this reaction with Bial's reagent is given by both glycuronic acid and pentoses, the result of the test with naphthoresorcin excludes the latter group.

9. Reaction with parabromphenylhydrazine. This reaction was negative. Neuberg (4) has described a crystalline hydrazine compound of glycuronic acid and p bromphenylhydrazine which is characterized by its insolubility in alcohol and its high specific rotation when dissolved in a mixture of pyridine and absolute alcohol. It has been claimed that this reaction constitutes the most positive test for glycuronic acid. Goldschmiedt and Zerner (5), on the contrary, state that the reaction is dependent upon conditions that are uncontrollable and that it is not a satisfactory test for glycuronic acid. My experience agrees with this conclusion.

10. Hydrolysis with dilute mineral acids destroys its anticoagulant action.

11. When boiled with dilute hydrochloric acid (1–4) and evaporated to dryness a white residue is obtained which is soluble in water but not in alcohol. Aqueous solutions of the residue reduce Fehling's solutions and give the reactions of glycuronic acid. The same treatment with nitric acid (s.g., 1.15) gives after evaporation a sticky residue, part or all of which is soluble in alcohol, together with a granular or crystalline inorganic deposit. Aqueous solutions of the residue reduce Fehling. Tests of these solutions with barium chloride and ammonium oxalate indicate the presence of sulphuric acid and calcium. If during the purification of the heparin, after treatment with Lloyd's reagent but before precipitation with barium hydroxide, some of the material is treated upon the water-bath with nitric acid (s. g. 1.15) and the solution is evaporated to a small bulk, as in the process of the production of mucic acid from galactose, crystals of calcium sulphate separate out.

12. Elementary analyses of the heparin for carbon, hydrogen and ash give the following figures O, 20.5 per cent; H, 3.75 per cent; Ash, 37 per cent.[2]

The conclusion drawn from these reactions is that the heparin is a glycuronic acid compound containing, as isolated, probably calcium and sulphuric acid in the molecule. The fact that it shows reducing properties only after acid hydrolysis would indicate that it is either a paired glycuronate or a condensation product of glycuronic acid. The low carbon percentage would favor the latter interpretation.

PHYSIOLOGICAL REACTIONS

The purified heparin shows the two characteristic reactions that have been described in previous papers, namely, an anticoagulant action upon blood and the property of causing an increase in antithrombin when added to plasma or serum. In concentrations of about 1 mgm. to 100 cc. human blood is prevented from clotting for 24 hours or longer. The blood seems to be preserved in an entirely normal

[2] For this analysis I am indebted to the kindness of Dr. Wintersteiner of the department of Pharmacology of the Johns Hopkins Medical School.

condition. The corpuscles settle rapidly as is the case with other anticoagulants and with the slowly clotting blood of hemophilia. Even after 24 hours the platelets may be found single, that is, there is little or no agglutination. If the platelets are pipetted off from the supernatant plasma and treated with water they quickly agglutinate and dissolve. For this reason the heparinized blood, when diluted freely with water, soon shows clotting. If, however, a fresh specimen of heparinized blood is centrifugalized at high speed for an hour and the upper layers are then removed and diluted with water, spontaneous clotting does not occur. The anticoagulant action of heparin is not destroyed by prolonged boiling of its solutions. Its aqueous solutions are also apparently highly resistant to the action of bacteria. A very dilute solution that was left over summer, a period of three and a half months, in a corked vial remained perfectly clear and exhibited the same anticoagulant action as when freshly prepared.

In regard to its antithrombic action it was found that heparin itself is not an antithrombin, that is, it has no effect upon the coagulating properties of active thrombin, nevertheless, when added to plasma or serum, it causes a marked increase in the amount of antithrombin present in these liquids, as determined by the effect of the mixture upon the reaction between thrombin and fibrinogen.

When the heparin is injected into the circulation of a normal animal in proper concentrations the blood is rendered wholly incoagulable for a certain period. In the case of a dog an injection of 1 mgm. to each 50 cc. of the estimated amount of blood (1/20) keeps the blood incoagulable for a period of about half an hour. In an hour the coagulability begins to return. Specimens withdrawn after this time may show imperfect clotting in 3 to 4 hours and complete coagulation later on (6 to 24 hours). After two hours specimens withdrawn may clot in 30 to 40 minutes and after three hours the coagulation of the blood is practically back to normal. During the first hour or two after injection the animal exhibits hemophilic oozing from the skin wounds made in the exposure of the blood vessels.

THE USE OF HEPARIN IN TRANSFUSIONS

The strong anticoagulant action of heparin, the absence of injurious reactions when it is injected intravenously, and the fact that its solu-

tions are very stable and can be readily sterilized by boiling suggested that the purified product might be useful in the transfusion of blood in human beings. Through the kindness of Dr. Longcope its applicability for such purposes was tested upon several patients in the medical wards of the Johns Hopkins Hospital. A solution was made of the purified heparin in 0.9 per cent solution of sodium chloride of such a strength that 1 milligram was contained in each 10 cc. of solution. The saline solution was made from freshly distilled water to avoid the products of bacterial growth that are known to be formed in distilled water that has been kept for some time. The solution of heparin was sterilized by boiling and enough was made at one time for a series of transfusions. In collecting the blood to be transfused it was allowed to run directly from the vein of the donor into a sterile flask containing the heparin solution, 10 cc. of the latter being used for each 100 cc. of blood to be transfused.

Ten transfusions were made upon six patients, one with primary anemia, the others with severe secondary anemias. In eight of the transfusions no reaction was observed, the amounts of blood transfused varying from 300 to 500 cc. In the other two cases there was a slight chill at one and a quarter and two hours after the transfusion, lasting for twenty-five to thirty minutes with a temperature of 102°F.

THE ANTICOAGULANT ACTION OF GLYCURONIC ACID

Since the heparin is probably a derivative of glycuronic acid it seemed desirable to prepare glycuronic acid and test its effect upon coagulation. For this purpose I was fortunate enough to obtain some Purree, the raw material from which Indian Yellow was formerly made, through the courtesy of Messrs. Winsor and Newton Ltd. of London. The Purree contains glycuronic acid as a magnesia compound of euxanthinic acid. The glycuronic acid was obtained from Purree by a modification of the process described by Thierfelder (6). The euxanthinic acid was obtained from the magnesia salt by the action of hydrochloric acid and was recrystallized from hot alcohol solutions. This acid was then hydrolyzed by one per cent sulphuric acid in an autoclave at a temperature of 125°C. The insoluble euxanthon was filtered off and the solution of glycuronic acid, after neutralization, was evaporated to one-third its volume before an

electric fan, filtered, and then carried to dryness on the water-bath. The residue was extracted repeatedly with a mixture consisting of alcohol 1 volume, ether 1 volume, and water 0.4 volume. From this extract the glycuronic acid was obtained by evaporation. The material obtained reduces Fehling's solution and gives the naphthoresorcin and orcinol reactions. The glycuronic acid as thus obtained has no anticoagulant action, but it was found that when heated to 250°C. it forms a dark-colored compound easily soluble in water, which has a very definite inhibitory effect upon coagulation. One milligram will prevent the coagulation of 1 to 2 cc. of human blood for 24 hours or longer. This compound and other modifications of glycuronic acid are now being studied from this point of view.

SUMMARY

1. A method is described for the purification of crude heparin which gives a product free from phosphorus and nitrogen. Its anticoagulant action for human blood is of the order of 1 mgm. to 100 cc. of blood.

2. The reactions of the purified heparin show that it is a carbohydrate body, apparently a glycuronic acid compound.

3. The use of the purified heparin as a safe anticoagulant for blood transfusions is suggested.

4. Glycuronic acid prepared from euxanthinic acid has no anticoagulant action, but on heating to 250°C. it yields a compound with distinct anticoagulant properties.

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THE EFFECTS OF GLYCOCYAMINE AND GLYCOCYAMIDINE ON THE BLOOD PRESSURE[1]

RALPH H. MAJOR AND C. J. WEBER

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Because of the marked pressor effect of guanidine, methylguanidine and asymmetric dimethylguanidine, and their very possible biological importance, we have recently tested the effects of a series of guanidine compounds upon the blood pressure. Many of the guanidine compounds, as pointed out by Alles (1), are quite toxic and in toxic doses usually produce a fall in blood pressure. Toxic doses of guanidine, methylguanidine and asymmetric dimethylguanidine may produce an immediate fall in pressure without any preliminary rise. This fact probably accounts for the negative results which some observers have obtained when investigating the pressor properties of these compounds.

We have been very much interested in finding that glycocyamine and glycocyamidine produce marked depressor effects. The presence of these two compounds has apparently not been demonstrated in the body, although there is some evidence that glycocyamine may be formed as an intermediate product in creatine metabolism.

Glycocyamine, it will be recalled, is guanidine acetic acid and resembles creatine very closely, which is methylguanidine acetic acid. Glycocyamidine is the anhydride of glycocyamine and bears the same relation to it that creatinine bears to creatine.

Baumann and Hines (2) found that the feeding of glycocyamine to rabbits and the injection of glycocyamine produced an increased output of creatine, but found no evidence for the methylation of glycocyamine by muscle or liver tissue *in vitro*. Such methylation in the body has been asserted by Führer (3) and others.

In the course of their experiments, Baumann and Hines injected doses as large as 160 mg. per kilo of body-weight into animals and fed

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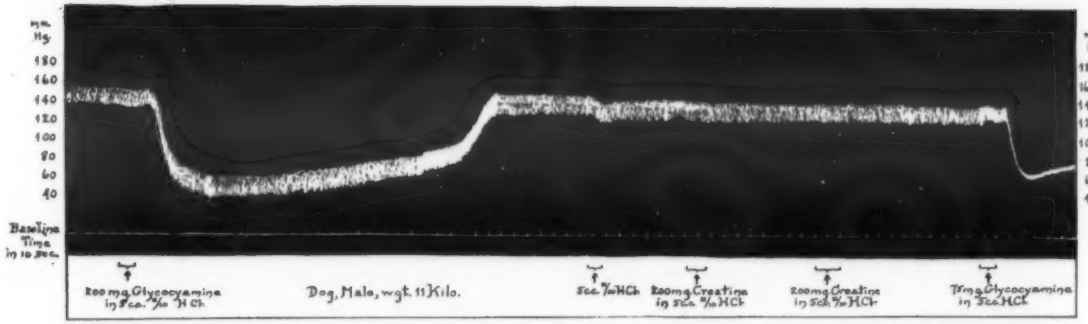

FIG. 1. TRACING SHOWING MARKED DEPRESSOR ACTION OF GLYCOCYAMINE WHEN INJECTED INTRAVENOUSLY

Glycocyamine dissolved in N/10 HCl. Intravenous injection of N/10 HCl and creatine dissolved in N/10 HCl without effect.

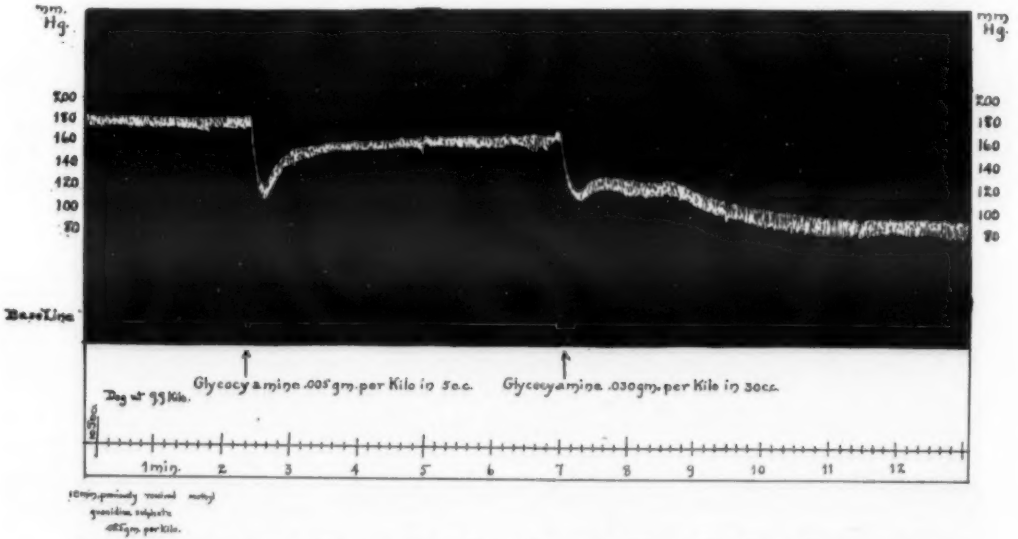

FIG. 2. TRACING SHOWING DEPRESSION OF BLOOD PRESSURE WHICH HAS BEEN ELEVATED WITH METHYLGUANIDINE SULPHATE

Dog receivd emethylguanidine sulphate 0.025 gram per kilo intravenously, 10 minutes before injection of glycocyamine. Glycocyamine dissolved in N/10 HCl and injected intravenously.

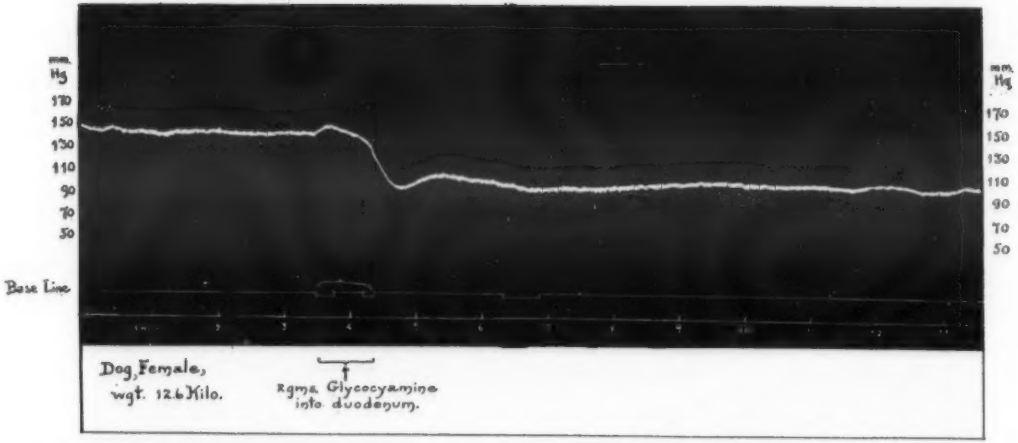

FIG. 3. TRACING SHOWING DEPRESSOR EFFECT OF GLYCOCYAMINE WHEN INTRODUCED INTO THE DUODENUM

This effect persisted until the termination of the experiment 2 hours later. Two grams of glycocyamine dissolved in 50 cc. N/10 HCl.

doses as large as 3 grams to a man weighing 62 kilos, without observing any toxic symptoms.

In our experiments, a dog under light ether anaesthesia was connected with a mercury manometer in the usual manner and the glycocyamine injected intravenously. In Figure 1 is shown the tracing from such an experiment, demonstrating the marked depressor effect on the animal's blood pressure following an injection of 18 mg. per kilo. Similar observations were made in three other animals.

Glycocyamine is also effective in abolishing the hypertension produced by methylguanidine. In Figure 2 such an experiment is shown. We have found that 1 mg. per kilo of glycocyamine produces a marked depression in the hypertension caused by the injection of 0.03 gram per kilo of methylguanidine sulphate, and from 4 to 5 mg. per kilo of glycocyamine usually reduces the pressure to normal. In several experiments, we have given intravenous doses of glycocyamine as large as 100 mg. per kilo without observing any toxic symptoms. This marked depressor action, as contrasted with the practical absence of toxicity, is a very striking feature of this compound. Experiments with glycocyamidine have yielded the same results, although we have not found this substance to be quite as effective against the rise in pressure produced by methylguanidine. Glycocyamidine in our hands has produced just as sharp a fall in pressure as glycocyamine, but the fall has not been of such long duration.

Glycocyamine also produces a marked depressor effect when injected directly into the duodenum. Figure 3 shows the profound fall in blood pressure which follows its introduction into the duodenum, an effect which persisted in the experiment for two hours and was unaccompanied by toxic effects upon the heart action or respiration. When introduced into the duodenum, it is also active in abolishing the hypertension produced by the intravenous injection of methylguanidine sulphate.

It is a matter of some speculative interest that methylguanidine and guanidine are both active pressor compounds, that guanidine acetic acid is an active depressor compound, while methylguanidine acetic acid is apparently without specific effect upon the blood pressure.

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SELECTIONS FROM THE LETTERS OF RICHARD D. ARNOLD, M.D.

Mayor of Savannah, Vice-President and Secretary of the American Medical Association

MEDICAL SERIES. PART II. 1834–1875

PRESENTED BY RICHARD H. SHRYOCK

From the Department of History of Duke University, Durham, N. C.

Nov. 5, 1854

Dr. E. D. Fenner,
New Orleans,

. . . . Having myself gone through the entire Epedemic from beginning to end . . . ., having treated hundreds of cases . . . ., having made my first post mortem on Yellow Fever in 1827. . . . . I feel that I ought to write out a history of our late terrible scourge. I am moreover a decided non-contagionist. The Fever here this year originated on the spot. As usual there are many *conclusive* tales as to its origin from some ship, but they will not bear scouting.

The first case of Yellow Fever occured in my practice not far from the center of the city; in a young Northern Carpenter, unacclimated. The weather had been intensely hot & he had been walking a very long distance daily in the sun. . . . . The next day I saw a case of Dr. Read's in a part of the city a long ways off from the first, & after that a second case of my own patients in another quarter. To be sure, each case was in a northeastern quarter of the whole city, at some point of which quarter Yellow Fever has always commenced, whenever we have had any cases of it. Occasionally I have met with Sporadic cases of genuine Yellow Fever.

If it could be generated at one time, why not at another? I received your pamphlets on Yellow Fever & was much obliged to you. . . . . I owe you for the second volume of the Southern reports. Winter before last a patient paid me a ten dollar Louisiana Bill. . . . . I now enclose it. Please pay yourself out of it & pay for whatever the

rest will on account of subscription to the New Orleans Medical & Surgical Journal. I want to know what is going on in a quarter so medically enlightened as New Orleans. Could I obtain a copy of Barton on acclimation? . . . .

April 13, 1855

Dr. Henry Bacon,

. . . . I have been so much occupied that I have not had time to write an account of our Epedemic, but I have full notes. *Our disease originated here*, beyond the shadow of a doubt. . . . . Local causes, such as filth, crowded population, ill ventilation, will add power to the virus & render it more fatal, but is not this the fact in all diseases? I concur fully in the report of the late Mayor. . . . . Dr. Hume of Charleston is simply *ridiculous*. If his *facts* as to Charleston are as *false* as his facts as to Savannah, then has he built on a Sandy foundation. . . . .

April 16, 1855

Dr. Rene La Roche,
Philadelphia.

. . . . It is only in the last two weeks that I have had time to put together my "disjecta membra" taken under the pressure of business during the summer. However, be they as slight as they may, they will reflect Nature & not echo books, for really I have no time to consult them. . . . . I have seen no reason to change my views as published some thirteen years since. The absence of all biliary secretion & excretion is the external characteristic symptom. The necroscopic results prove this to depend on a peculiar derangement of the Liver. Black Vomit is blood passed through the coats of the Stomach. The Fever is distinct & specific. This is a summary of my creed. I was pleased to see by the Journals that you were engaged in a work on this disease. . . . .

I will leave Savannah for your city in the Keystone State on the 25 inst. & expect to stop at the Gerard House. I anticipitate great pleasure in meeting old friends. In fact Philadelphia stands next to Savannah in my affections. . . . .

June 29, 1855

Dr. C. R. Gilman,
New York,

It gives me great pleasure to reply to your inquiries concerning Dr. J. Le Conte, if you mean Dr. John Le Conte, Pofessor of Chemistry in the University of Georgia, at Athens. It is enough to say that I exerted any & every influence it was in my power to do to procure him that position. He settled in Savannah after having been graduated in New York, I think in your school. He was a great aquisition to the literary circle of Savannah & I parted from him with reluctance.

In our Medical Society he was a ready, fluent & forcible speaker, & seldom failed from his extensive reading to impart information on the subject discussed. One of my students sat under him at College & frequently has spoken of him as an excellent lecturer. The Le Contes are a family remarkable for their devotion to literary & scientific pursuits.

July 18, 1856

Dr. John Eckhard,
17 Branch St., Philadelphia.

I wrote for our State Society an Essay on the Relation between Yellow & Bilious Fever. At the request of the Society. . . . . it is to be published in the Augusta Journal. I carried up my paintings from nature, of the colour of the livers in the two diseases. . . . . I wish to get them lithographed in colours to accompany my paper . . . . . The object of writing you is to ascertain at what cost you could get the five paintings done in coloured lithographs. . . . . .

My essay is not very elaborate, but as it is devoted to one point & that point is elucidated by a personal experience going over many many years, I think it will not be uninteresting to the medical public.

I flatter myself I have fully *proved* two things, the *identity* of the Yellow Fever which has appeared in Savannah from 1820 to 1854, and its being an entirely distinct disease from Bilious Fever. . . . . I forward the paintings by my friend Octavus Cohen, who starts tomorrow in the Keystone State. . . . .

March 10, 1857

Dr. Thomas S. Kirkbride,
Pennsylvania Hospital for the Insane, Philadelphia.

I have a near friend . . . . who is favored by Providence in mind & fortune, but who mars all his gifts by the terrible vice of intoxication. He is what I call a periodical drinker, & which, years ago, I classed as a kind of periodical insanity. No one knows these cases better than you. Latterly the periods of soberness have become shorter & shorter. I have long entertained the idea that in cases of confirmed bad habits the Law ought to allow the relatives to place the Subject in an Insane Assylum, to try if a forced abstinance of not less than a year, might not eradicate the vice. I write to beg your opinion because the gentleman in question is willing to try the experiment, & his only sister feels & knows it is the last hope of reform. Kind, amiable, liberal, intelligent, when sober, he is a devil when drunk. . . . . I confess I have but little hope. However, I write to ask you if you have tried to cure such cases &, if so, with what success & to ask your advice as an Expert in Insanity.

The means are ample to afford any expense which may offer a fair chance of reform.

July 17, 1857

Dr. F. M. Robertson,
Charleston, S. C.

Yours of the 15 inst. came to hand today. I certainly thought I had sent you a copy of my essay. . . . . I recollect & have among my archives your report on the Yellow Fever of August in 1839 & I would consequently look to you as one whose experience enabled him to judge advisedly & one whose opinions I would more willingly learn, as the Medical mind of Charleston seems to have undergone a strange change compared with former years. I had the pleasure of entertaining Dr. Hume (?) as my guest this summer, much to the amusement of a young graduate of our College, my quandam private pupil. I gave a medical dinner party to the Doctor. My pupil, after having been introduced, said aside to me, "Is that Dr. Hume of Charleston?" "Yes," I replied. "Is that the man whom in your lecture you called

the Archbishop of Contagion?" "Well", said I, "I do not recollect the term but it is well merited, & it sounds very like me". . . .

You are right in calling the notice of the Charleston Journal an "imperfect" one. After having read my essay you will perceive that I do not at all *argue* the etiology of Yellow Fever. . . . . As to his sneer about malaria, he shows only his own ignorance. . . . The man in our locality who would deny that low grounds, having the two elements of vegetable matter and moisture, *do not* give off a specific malarious fever breeding exhalation, would be laughed at. . . . . It is the A B C of our experience as medical men. Let Dr. Nott (which I *doubt*) and Dr. Cartwright (who is no scientific authority) vouch, according to the Reviewer, for the healthiness of Louisiana swamps. I appeal to you, as an old resident of Georgia, if such healthiness obtains in Georgia Swamps.

With my essay I send you a catalogue of our Medical College. As far as numbers are concerned we do not come on well. But for energy, for hard work, for capital opportunities, anatomical & clinical, we stand well. We have a fine college edifice built & owned by ourselves. I like the plan *better* than any I have ever seen. . . . . Two years ago we turned Dr. H. L. Bird out of our Faculty. . . . . To revenge himself he started a new College. Undoubtedly this has in various ways injured us as he has no hesitation in resorting to any means to exalt himself & injure us. . . . . The chairs of his (Oglethorpe) College have never been filled. . . . .

As an educated man & one who has the *standing* of the profession at heart, I beg to call your attention to the stand taken by our college in relation to Summer Courses. I had full talks with your professors during my recent visit to Charleston. . . . . I am proud that our college has taken this ground. If it be not sustained I honestly believe it will be the severest blow to Medical Education, attenuated as it is, that has ever yet fallen upon it, & God knows that in its present ricketty condition a straw could pierce it. For one, I hope that in my private & professional capacity I have endeavored to uphold the standard of medical education. Comparatively young, I was one of the pioneers of the American Medical Association. Alas, what can we expect from that! I confess my dream in that quarter is at an end, unless new measures should be devised. Thanking you for the opportunity of explaining my views & those of our school, I remain. . . . .

July 18, 1857

Dr. C. H. Sackrider (?)
Mason, Michigan.

It gives me much pleasure to comply with your request to send you a copy of my Essay on the Relation of Yellow & Billious Fevers. . . .

I beg to call your attention to our stand in relation to Summer Courses. This subject will be fully brought before the next meeting of the American Medical Association. . . . .

July 18, 1857

D. M. Reese, M.D., L.L.D.,
10 Union Square, New York.

Enclosed you will find an advertisement of our College which we wish inserted in your August Number. . . . . I shall send you one of our circulars. . . . . We have taken the first bold, unequivocal stand against a growing abuse, viz. taking a winter student, hurrying him through a Summer Course, & turning him out a Doctor in less than a year from the time he heard his first lecture. This has been done by Oglethorpe College here. . . . . The Atlanta College avows & defends this course. Sir, you are one of our Pilots. . . . . You won golden opinions at Nashville by your defence of our Profession as it was formerly educated. Has not that day passed away? When schools can act this way & Professors in open Association talk as some talked are we not falling upon evil days? As God is my judge I speak for the Profession at large & not for our College. . . . . We claim the credit of having first spoken out in meeting. Will the profession remain apathetic & think this a dispute between schools? I hope not.

August 1, 1857

Jacob Waldburg,
Clarksville, Ga.

In accordance with previous arrangement I left the City with Dr. Wayne & reached St. Catherines at 4 P. M. We found twelve patients from Macqueens & South End placed in the Moting (?) House as a temporary Hospital. . . . . Our first remedy was moral, to endeavor to infuse confidence & to remove the alarm which evidently existed on all hands.

In the evening Mr. Gregor came over & from him & Phebe we endeavored to trace the history of the rise & the symptoms of the disease. I must say, & I am loath to believe in importation & contagion, that I have never know more direct, posative, & unequivocal testimony as to the origin of any disease. Here is a sequestered Island, having little communication with the world, with a population rarely in contact with any other. A new comer arrives, falls sick, has a disease so marked that the difference between it & the diseases ordinarily met with on the Island strikes every observer. Now when the symptoms are detailed to professional man he cannot fail to recognize genuine Typhoid Fever. The nurse attending him is attacked with a similar disease, then two children about her, & so it creeps from one to the other. . . . .

Of course our directions were obliged to be general. Had we given a regular detail, it would have been applied to every case indiscriminately. . . . . Our principle directions were in relation to Hygienic measures & avoidance of strong exhausting treatment.

We wrote a pretty full letter of instructions for Mr. Gregor & enforced our views more directly on Phebe. . . . . I think there was a better state of feeling among the negroes when we left & Mr. Gregor was evidently much relieved by our visit. It was natural that he should have felt that a heavy responsibility was taken from him. My reliance, however, is on Phebe.

I think the worst has passed. You will have heard from other sources of your crops. . . . . One afternoon we rode to the beach. How delicious, how balmy, how refreshing the sea breeze! How could you ever have preferred your mountain air to it?

Oct. 8, 1858

Dr. C. R. Mowe (?)
Weston, Webster Co., Georgia.

Your letter of the 3rd of September reached me just at the outbreak of our epedemic & I must plead constant occupation as my excuse for the delay in answering it. Fortunately for Savannah, the mortality has been extremely small, else she would be sitting in Sack cloth & ashes. The epedemic has been of the Dengue or Break bone type, occasionally cropping out into fatal Black vomit. In the next number

of the Journal I propose to republish from the Charleston Journal of May, 1851, my article on Breakbone or Dengue Fever. Ever since 1854 I have been satisfied that it is only a mild type of Yellow Fever. The experience of this year confirms me in that opinion.

August 21, 1859

Professor M. K. Taylor, M. D.,
Galesboro, Illinois.

It gives me pleasure to forward to you a copy of the article referred to by you, also of one on the Identity of Dengue & Yellow Fever. . . . . I am not much of a writing theoretical man. I have led too active a professional life for that. Hence perhaps I am inclined to pin my belief upon those who have been most at the bedside, in opposition to the mere Microscopist or analytical chemist, each of whom is useful to elucidate truth but necessarily each (not-?) an oracle. I refer you to my essay simply as records of what I have observed at the Bedside & in the Dead Room.

March 4, 1860

Dr. Alfred Stillé,
Philadelphia.

Yours of the 24 ult. came duly to hand. Certainly our National Association has conferred one great advantage on me, viz. the opportunity of forming the personal acquaintance of so many of the bright lights of our Profession in our Union, whom otherwise I would have known only by reputation. I had known you before 1846 as a writer in *The* Journal; since I have had the pleasure of a personal aquaintance, it has enhanced my gratification in reading your contributions to our medical literature.

I have never yet visited Philadelphia without calling on you. Now I have said enough. It would give me the greatest pleasure if I could in any way assist you in attaining the object of honorable ambition at which you now are striving. As a mere provincial, a kind of outside professional Barbarian, I feel flattered that you should have thought I might in any way contribute to that end. . . . . Somehow or other I always looked upon you as one of the heirs to the Chair

of Practice in the University.[1] Your turn of mind & your studies tended in that direction. Your apprenticeship in the Pennsylvania College will & must have its weight. Now you have all scattered, permit me to repeat what I conscientiously said two years since, viz. that as a whole the Faculty of Pennsylvania College was superior to any other in Philadelphia.

Honest medical teaching I find devilish hard work. The profession is going to destruction in Georgia from the utter want of principle in some of our Colleges, who look upon filling their benches & their pockets as the end & aim of incorporated Medical Colleges. I have one consolation, we own our College & apparatus & do not owe a cent. But I am tired of lecturing to small classes & feel very much like quitting, if I could do so with justice to my colleagues.

I do not know whether I can get off this summer. I am Mayor of the city and do not like to be absent as I receive a Salary, unless on City business or for purposes of health. . . . .

Remember me kindly to my friends in Philadelphia, who always are uppermost in my thoughts when I think of the North. Why do not some of them take an occasional trip South? I can always furnish a bottle of Madeira to the temperate & Iced water to the abstinent, with an addition of Sponge cake and coffee.

July 13, 1860

My dear Mary,

. . . . I had a delightful time at the North, & not the least pleasant time at Boston. I was elected first Vice President of the Sanitary convention & as the President, Dr. Bigelow of Boston, was too old to perform the duties they devolved on me all their concomitant dignities. . . . .

Oct. 20, 1860

Dr. W. H. Mussey, Cincinnatti, Ohio,

Your letter of the 15 ult. inquiring after the publications of the Transactions of our State Society came duly to hand.

There is no completed set. One or two pamphlet publications of the transactions have been made, but for many years the simple

[1] Presumably the University of Pennsylvania.

record has been published in the Augusta Medical Journal, and so also have been the few papers which have been contributed. A file of that Journal would give you a more connected view of our Society than any other source.

I am sorry to say that the Society has as yet accomplished *nothing*. A few men in the up country have kept the meetings confined principally to one section of country and consequently to one set of men. Had they acted & written, for one I would have said Godspeed. But they *have not*. . . . .

Jan. 3, 1861

Dr. C. H. Colding,
Vienna, Dooly Co., Geo.

. . . . I have heard a good deal of Diphtheria, but have seen but two cases in the last two years. These I treated successfully by caustic and calomel as you did yours. I combine Powdered Ipecac with the Calomel. Many cases of ordinary———sore throat are, I posatively know, *called* Diphtheria. Diphtheria is, as its etymology denotes, *membranous* sore throat. It prevailed here epidemically in 1848. . . . . In advanced malignant cases I would try Muriat Tinct. of Iron and stimulants. . . . .

Feb. 22, 1862

John Richardson, Esq.

Yours of the 31st ult. came to hand last night. Its receipt gave me pleasure because it enables me to answer you authentically on the very points which I have been solicitous to bring before the Executive committee of the Georgia Relief & Hospital Association. . . . .

When the Faculty first determined to offer their buildings & their services, they expected to obtain the services of some young physician, a graduate, who would reside in the Hospital & superintend all the arrangements, hygienic & medical, keep the books, see that the medicines were given, etc. This hope of obtaining one was not abandoned until we had been in operation over two weeks. Mr. Wallace was acting Steward & his carelessness & incompetency consumed my time & wore out my patience, & I said openly I could not continue on with him. Mr. Miller applied to me to get some employment. Knowing

him to be a good penman & accustomed to official accounts I thought he would suit, & you were kind enough to appoint him. Now to show you that I expected an Apothecary after having given up all hope of obtaining a resident Physician, I offered the place to Mr. Wallace, because I thought (& still think) that if he attended to his business, he could "mix medicine to the extent of our Pharmacy." He agreed to accept the remuneration to be decided by the committee. This was Sunday. On Monday & Tuesday (6 & 7 Jany.) he was absent from 3 o'clock P. M. to 8 P. M. I determined not to stand such conduct. Mr. Miller had been occupied almost every minute in receiving & placing in the Wards some forty patients, & if it had not been for the assistance of some Medical Students, the medicines for these two days could not have been put up. On Tuesday night I wrote to Mr. Wallace dismissing him & on Wednesday morning I reported facts to Mr. Stoddard & explained the necessity of an Apothecary. . . . . I understood all my colleagues to coincide with me in the necessity of an apothecary in the absence of a Resident Physician. . . . .

Now the compensation of thirty dollars for the labour & confinement to duty for Steward & Apothecary is really too little. When you go to the Hospital ascertain for yourself the amount of writing Mr. Miller has done & the accounts he must keep with the Confederate & State Governments, in order that the Hospital may receive compensation for rations of the patients. . . . .

I am entirely satisfied with Capt. Miller. . . . . His general management shows him to be a very competent man for his present situation.

R. D. Arnold, M.D.
Medical Director of the Savannah
Medical College Hospital.

Oct. 8, 1866

Miss Fanny Mims,

Your letter postmarked Emmetsburg came duly to hand & this is the fourth time that I have sat down to answer it & I shall do so, however short my letter may be, as I know you are all anxious to learn authentically the state of health of our city. Since the 28 July

we have had cholera on the outskirts of the city but as heretofore it has made no lodgement in our centre. A few cases have occurred in the middle of the City, but there has been but *one* death in any circle that one knows, viz., that of Mr. Benjamin Whitehead, who was my patient and the only one that I have lost from that disease this summer. The principle mortality has been amongst the Blacks and the principle locality for the disease, the Lincoln or Freedmen's Bureau Hospital Southeast of the Savannah. Of those Whites who have been attacked almost everyone was down on or a little above the water level. My cook was attacked in my yard and had Ricewater discharges for two days and a narrow escape from death. I do not yet believe in its contagion. I believe the poison floats in the atmosphere & that mere proximity to a sick person does not increase the danger of taking it. Stating this authoritatively I prevented a panic in my yard & Ellen boldly nursed her as if she had been her slave, instead of being "*nobody's nigger but her own.*" Isaac her husband was permitted to devote his whole time to her, & her wine etc. was furnished from the house. I should like to have had one of the puritanical, hypocritical, self-satisfied Pharisees of Massachusetts to have looked in from any corner he might have selected for his espionage. Perhaps he might have induced some of the lying Radical Journals of his self-exalted State to have astonished the South by telling the truth about the condition & treatment of the negro of the South.

In the beginning of the season there were a few scattered cases of Yellow fever but they had so sequents. The season has been a good one, many refreshing showers and much electricity. I never had the slightest apprehension of its becoming epidemic. The course of the disease has been such as to confirm more fully my often written views as to this fever. Its spread here depends on the long continued heat of the weather & it originates in this place. I consider the season to have been a very healthy one. Whilst as usual I have had many cases, they have been very manageable & with very little fatality.

I have been this particular because I have heard that some exaggerated reports have been written from this city, & I know that there is a perfect panic all over the up country. Ellen & the children have been quite well & remain so. While my cook had the cholera I had some premonitorys, but having been convinced in 1834 that this stage

of disease is the curable one and that when cholera is in the atmosphere generally an ounce of prevention is worth a pound of cure, I soon checked it. Now I have had a good many cases of Diarrhea, have several times been called up in haste at night by persons scared almost to death, but poor Whitehead is the only case I have lost & I know authentically that he had been sick three days before I was called in to him. He was in a collapse on my second visit. I hope your Mother continues to improve & that Cecilia has recovered from her accident. Rebecca I believe has turned [?] India Rubber. How are my dear friends Dr. and Mrs. Hays? Tell the Doctor I read and reread his admirable article on Cholera in the News & used some of his old Thunder to strike the high vaulting ambition of some of our young medical men, who take their medical opinions from the last London Periodicals, as the cameleon his hues from the colour of the last branch on which he has basked. . . . .

Oct. 8, 1860

Miss M. W. Houston,
Madison, Ga.

Your two letters from Madison came duly to hand. Although there has been no unusual amount of sickness you know I have always enough at this season of the year to keep me very busy. I attended to your request contained in your first. There were four quarters rent due and one re-entry, so I paid them all to save a second re-entry. Miss Welman told me she had written to relieve your mind of the apprehension excited by the absurd reports circulated in the up country about the health of Savannah. I have seldom known a healthier season. The Cholera with a very few exceptions has been confined to the Blacks and the outskirts of the city, its principal habitat being the Freedmen's Bureau Hospital. I have lost but one patient, unfortunately *the only subject* of any social standing who has died, viz., Mr. Benjamin Whitehead. My cook Fanny had a severe attack & she may thank God that she was an independent Nigger "living in her own house." Prompt attention & Ellen's nursing saved her life. Yellow Fever died out with a few sporadic cases early in the season. The mortality is certainly great among the Blacks, but I am satisfied that belongs to their new status of being "nobody's niggers but their own."

A comparison of the mortuary records of the five years preceding the war & the five to follow will solve a problem in Sociology in a way that will astonish the negrophilists who may be alive at the end of the last term.

Nov. 11, 1866

Dr. D. W. Hammond, Macon, Ga.

Your letter of the 8th ult. came duly to hand. As your letter refers to so serious a matter as a change of your residence I shall reply in order, premising that of course you are well known to me personally as well as professionally, for I first met you at the organization of the State Medical Society in 1849, & your career as a medical man since in Macon, for you did not then reside there, has been quite familiar to me. First, I doubt the practicability of forming a copartnership with any established Practioner. The profession is crowded & the altered status of the negro has materially affected (& injuriously) the income of every Physician. If you come you must make up your mind, I think, to launch your own bark on the sea of experiment. Your well deserved reputation as a Lithotomist would benefit you but little here, unless your patients followed you, for calculus is a disease so rare that Dr. Waring told me (the old Dr.) that he had never known of a call in his experience, & but *two* have ever come to my knowledge in thirty-six years practice. Your statement that you are considered to have the best pay practice in Macon is fully believed by me from what I have always heard of you. Recollect, my dear Doctor, a Doctor is like a tree, the longer he has been in one locality the deeper his roots have struck. You forget or do not allude to the fact of my having met you in consultation in the call of my friend Col. De Graffinried during the war, and of course as you were his family Physician I need no references. The Roberts who are my patients spoke often of you after their return from Macon.

It remains for me to give you, as you request, "a full & frank statement of the prospects."

First, living is exorbitantly high. You cannot get any decent board under fifteen dollars a week per head. Should you wish to keep house, houses are very scarce & rent extortionate. This of course refers itself to your finances.

Second, all new comers must build themselves up by degrees, no odds how old in practice in other places.

Our profession is in excellent condition here. I have laboured & I flatter myself not unsuccessfully as President of the Georgia Medical Society (our Local Society) to elevate our ethical & professional Standard & a man of your standing in the profession would command & receive every due attention.

P.S.

I shall destroy your letter without exhibition to anyone, so if you wish to open the subject with anyone else you must open a new correspondence. This, as you will perceive, leaves the whole matter in your own hands.

Jan. 1, 1868

Dr. D. W. Hammond, Macon, Geo.

. . . . My address of last year embodies a history of our College, that of the 8th the history of our Society. Our College is doing better this year. We have twenty seven against ten last year but it is up hill work. Ten thousand dollars could not repair the damage done us by the Federal troops.[2]

March 28, 1868

Dr. Henry M. Fuller
Beaufort, S. C.

. . . . I write this fully for another reason. In these days of what I call Sanguiphobia the pendulum has swung clean to the other side. If we bled too much formerly, I firmly believe we bleed too little nowadays. We have certainly lapsed back into Brunonianism[3] in its naked priority. But judging from my own experience, and certainly it would be mock modesty in me not to claim a very large one in

[2] After Sherman's occupation of Savannah the Medical College building was occupied as a United States hospital; and upon the removal of the troops the federal medical officers carried off the equipment, museum specimens, etc. See F. D. Lee and J. L. Agnew, *Historical Record of the City of Savannah*, (Savannah, 1869) p. 165.

[3] A popular eighteenth century theory that diseases are caused by excess or lack of stimulation, and hence indicate narcotics or stimulants.

Hospital and private practice, there is a decided change in the character of the disease since I first began to practice thirty-eight years ago. I am glad to find from Aitkin's (?) recent work, that such high authorities as the late Dr. Alison and Sir Thomas Watson are of the same opinion, and I am content to abide by my own conclusion and the result of my recent experience *whenever I have deemed* V.S.[4] advisable, and leave Bennett and his followers (I would have added Todd, but he is dead) to congratulate themselves that our former bleeding was an entire mistake, and that their present stimulation is the result of higher information. I must tell you a pretty fair thing on one of my brethren here which occurred about twenty months since. Our medical Society meets weekly. V.S. and local blood letting were the subjects to be discussed (as per programme). I advocated the views expressed above. The gentleman in question said he carried a lancet but it was solely to lance abscesses. About five days subsequently I was roused up a little before five A.M. with a call to visit him medically. I found Dr. Kollock in attendance on Dr. Harry (the gentleman in question). He had been so for nearly twenty-four hours. Flax seed enemata, and calomel and morphine had been freely exhibited and a very large Blister covered the whole abdomen. His condition was as follows. The abdomen was swollen very tense, tympanitic at every point and very painful on the slightest pressure, his position was bolt upright as the intense pain kept him from swinging backwards or forwards and the bowels were constipated. The pulse was excited, hard, but not remarkably full. On retiring to consult I said to Kollock, "You know what you and I would have done with such a case thirty years ago," making the sign of V. S. "Yes" he replied, "but he is so opposed to Bleeding". "That is nothing to me", I rejoined. (I like to bullywragg a Doctor.) "Well you must do it then." "Very well." Enter two doctors, Arnold loquitur: "Harry, Kollock and I are of a unanimous opinion that you must be bled." I believe I had a slight twinkle in my eye. "Well," said he, and stretched his arm out. After the blood was stopped (I always bleed by Marshall Hall's rule) the patient being upright, he lay down for the first time since eleven of the preceding night. At

[4] Presumably "venesection."

one oclock that day we repeated the V. S. His bowels had been opened between our two visits. I was almost certain this would follow because I am convinced that the constipation of the bowels is dependent on a spasm of the muscular coat, and I had relieved just such cases as Harry's over and over by the same means. Now let me state a fact. Some years ago every spring presented this form of disease, for several springs in succession. I had not met with a case before Harry, for more than 10 years, and I have not seen one since. The truth is, we are led away and astray by names. Debility is relative. We must govern ourselves by the state of the Patient, which is determined by the state of his organs and tissues and I shall maintain that Bronsons [?] with all his ultraism was a genuine and efficient Medical Reformer. I know you are measurably out of Harness, but I hope I have not bored you with too much of the shop. As you wrote me you might yet be called to exercise our noble art in some case of emergency, I thought it would not be intrusive to give you some of my experience.

Although I have taken a part in local politics, as I think every educated man ought to do, my profession has ever been my guiding star. Although the classes of our Med College are small, the labour of preparing lectures is just as great, if a man respects his own reputation and duty, as if the classes were large. I have just delivered my eleventh course on Theory and Practice and July next will complete 38 years during which I have been connected with our Hospital. And to leave my *ego* behind, I wish no acknowledgment beyond your kind feelings, of the assistance rendered you, an assistance so slight that it derives its value solely from the circumstances by which we are all surrounded.

We in Savannah have every reason, badly off as we are and worse off as we are destined to be, to be profoundly thankful that we have escaped the overwhelming desolation which has overtaken the gentlemen of the Seaboard and their families. It makes one sceptical of a Providence at times. I have always said and believed that one of the elements of the bitter hatred and vindictive malignity of the majority of the Northern people against the South was the superiority of our general Social state. In one word, we were too feudal to suit codfish aristocracy, Petroleum wealth, or Shoddy Show.

I send you some Newspapers not for the news, but because they contain some articles of mine, political and literary. You will see I am not an idle man, My present impression is that the Northern people will submit to anything, that the minority there is in as helpless a condition as we are, for all power is in the hands of the Radicals and will remain there for a year; and in the meantime the Constitution will have been driven to splinters and all Liberty destroyed, an irresponsible legislature having totally usurped and abrogated the two coördinate departments of the Executive and the Judiciary.

July 24, 1869

Dr. B. A. Clements,
New Orleans, U. S. A.

Fifty times have I looked up to my shelf & said: "Well, it is time to send my pamphlets on to Dr. Clements," & fifty times have I failed to do so. I have been to New York since I saw you, & there were several vessels at Quarantine there with Yellow Fever on Board. So after all this scourge of humanity will, I am afraid, always combine to be an interesting subject for the Physicians in the Southern portion of our Country. Yellow Fever has been prevailing to a greater or less extent along the Gulf coast & amongst the West India Islands since May. I do not believe in its contagion or its importation by persons, but if the germs, for they must be material, exist for a long time in the Gulf or among the Islands they may float on the atmosphere over the Gulf Stream & by favoring winds be blown into our Atlantic cities, there to propagate if the season is favorable, that is if it be very hot & very dry. Or, if we have very hot weather long continued as we had in 1854, without any electricity (for there was not a thunderstorm from the beginning of June out) the germ of the disease will germinate in any city as low down as Charleston, Savh, or N. Orleans. In 1862 when we were blockaded *completely* I lost eight cases of Black vomit or genuine Yellow Jack. . . . .

July 3, 1870

Dr. Meredith Clymer
135 Lexington Ave.

. . . . The old Faculty of the Savannah Medical College have resigned. Three of the old faculty have gone into the new organiza-

tion. I declined accepting the Emeritus Professorship of Practice, as while I wish it well, I do not desire to pledge myself in such a way for it as I would were I to allow my name to appear in that position. I resigned avowedly & openly from the inefficiency & laziness of our Professor of Anatomy. There are some of the new Faculty with whom I would not care to be associated. Six of the old Faculty own the entire building and apparatus. We built it as the Savannah Medical Institute under an act of incorporation. Having built the building & furnished the apparatus the Trustees of the Sav. Medical College who had a charter & nothing else, elected the Faculty in 1853 & of course chose the owners of the building, with opposition of course from some of our medical Brothers, but we had the inside track having planked down in 1858 (?), nearly 3700 dollars.[5] In that year, I did a little lobbying, as Augusta & Atlanta Colleges were knocking at the door of the state Treasury, which in those good old Democratic days was full, & I joined giblets as Bennet says & the State gave the Trustees 15000 dollars. They gave it to the Institute & we purchased additional apparatus to the amount of nearly $2000, and appropriated the remainder to paying off encumbrances & setting the Property entirely free. I have, however, been working in vain as to building up the college. We have never recuperated from the war. Our young men of the rural districts who were our pabulum, have been too restricted in their means. We had a very fine Museum & apparatus estimated at about $10,000. It was destroyed with a few exceptions, say $1500 worth at the maximum. Don't you think this was the pursuit of knowledge under difficulty?

I have this consolation. Although my classes were small I had always a few intelligent fellows amongst them before whom my pride would not permit me to stumble & I became much more of a student than I would have been without such a stimulus.

After having resigned, the six owners being desirous of knowing what valuation to put on the property, employed the City assessors

[5] The "Savannah Medical Institute" had received this charter as early as 1838. Its board of trustees was really merged with the new group, which actually put up the Medical School, through the election of Arnold and one other member of the latter to the board. Arnold was chosen president of the board of trustees, as well as professor of theory and practice. See Charles C. Jones, et al., *History of Savannah*, (Syracuse, N. Y., 1890), pp. 453–455.

to appraise the Property. They did so, valuing it at $30,000 should it be continued for educational purposes and at $21,000 should it be sold to be cut up into dwelling Houses, as the latter would involve of course the expenditure of much money. Two of the present faculty own respectively a seventh and one quarter of a 7th (four of us having bought out the estate of Dr. West in 1860). The remainder of the new aspirants for Professional Honors could not raise any money. So we agreed to let them have everything for one year, on their paying the Insurance of the building. In the meantime we have offered [it] to the City for $14,000, provided it shall be kept exclusively for a Medical College. The idea is for the City to buy and transfer to the Trustees for the purpose of Medical education. I know the College has had a good effect on our isolated Fraternity and I would wish to see it prosper. The Faculty owning the College buildings hampered them and the Trustees. The majority of us were fools enough to let a Jackass buy in and once in, he was like the old man of the sea on Sinbad's shoulders, the only way to get rid of him was to dissolve ourselves.[6]

My freedom from Professional engagements will, I hope, enable me to do a thing I have for years wished to do but could not on account of my professional duties here, viz. to visit New York and Philadelphia in Oct. and Nov. when the lectures first commence and devote myself to an entirely medical tour.

So I shall live in hopes of seeing you in the flesh in October, gaining as I always have new knowledge, and a fresh impetus in what after all its toils, turmoils, and troubles, is really the most philanthropic of all callings and far ahead of the miscengenated Theology of the day.

July 3, 1871

Dr. E. S. Goullard,
Louisville, Kentucky.

Enclosed please find P. O. 18137, being the amount of subscription to your journal from Ist. inst. for one year in advance.

[6] The building was sold in '71 and lectures given in the hospital. The college continued to function until 1881, when "on account of death among the faculty and an apparent lack of interest in the institution by the resident profession, the college suspended work," Jones, *op. cit.*, p. 455.

I cordially endorse the tone and conduct of your Journal and I think it ought to be supported as an exponent of the Southern Medical Mind. But my dear Doctor, you must acknowledge that we move in a provincial circle, not because we are Southerners, but simply because we are outsiders of the great Central body. Is not Philadelphia paling before New York? What one of us takes a Boston Journal, high in intellect and medical culture as Boston is? Still New England Men ought to, and do, support Boston Journals. No prominent Journal to my knowledge is published elsewhere in New England. Let us then support our sectional (if I may use the word) Journals, let us contribute our experience of diseases peculiar to climate and Locality (to which latter I attribute great importance). But let us reap the benefits of a recorded experience in large cities, which experience can be aquired only in such extended spheres. Compare our large cities with the field of observation in Europe and they dwindle into comparative insignificance. Where in this country, in this once Grand United Republic, where, I say, could such opportunities for observations in Embryology be afforded as have been in Germany?

Admirable for condensation and for lucidity as are the researches of my learned friend Dr. Meredith Clymer in the diseases of the Nervous System, is he not obliged to base his instructive lectures on results obtained from post mortem examinations made in the Hospitals of Europe? What is the difficulty? I reply the prejudice against *practical anatomy*, which is greater in new and sparsely settled countries in a direct ratio to that sparseness. Let us then carry out carefully clinical observation (never to be cheapened by comparison with any other mode of observation.)

I go tomorrow to Macon to attend a convention of Physicians to be held on the 5th in relation to the recent hunkermongering of the Atlanta Medical College at the recent meeting of the Georgia Medical Association in April last, as the Atlanta school has in point assailed the Savannah Medical College. I may hereafter buy a place in your Journal for a statement of facts, which will go far to prove if sustained that the Atlanta Medical College is and has been in our State the greatest Enemy to a liberal Education of Medical Candidates which has ever existed within its limits.

If you can make any use (by elimination) of what I have written, you are at liberty to do so.

Oct. 11, 1871

Dr. Meredith Clymer,
4 East 29th St. N. Y.

. . . . This summer has been a remarkably healthy one with us. This corroborates my experience, that a very wet season is a healthy one. Why? Because the excessive heat is tempered down and you get rid of the great factor of malaria and Yellow Fever germs.

Let a season be rainy until the end of July, then let the rays of the August sun pour down on the moistened earth and the decaying vegetation, and you will certainly see a sickly time for malarial or, what I prefer to call them, Paludal[7] fevers. (I said this years ago in my lectures).

There was a great panic here on the occurrence of Yellow Fever in Charleston. Since our devestating epidemic of 1854, the people at large have turned fools as to the contagion of yellow fever and I have no desire of stemming the popular torrent. I began to appreciate the good sense of the Old Churchman "Si populus vult decipi- Decipiatur". Asses that believe in the tidal wave and the honesty of Ulysses Grant ought to be left to chew their thistle unmolested by argument. My friend the mayor, Col. John Screven, sent for me to advise with, on the first official notification of the appearance of the disease in Charleston. The old women in breeches were frantic and shrieking for stopping the cars between this city and Charleston. I told him that even I, with my positive convictions as to the non-transmissibility of the disease by person or luggage, if acting as Mayor would feel myself compelled to yield to such universal prejudice. But, I said, the best quarantine is Hygiene. Acting on this hint, he took measures to make Savannah as clean a city as can be found anywhere. Privately I expressed my opinions freely so as to allay Panic. I began the study of medicine in 1821, just six years after our noted Epidemic of 1820. My Preceptor was Dr. Wm. R. Waring, who had been through the whole Epidemic.

At that time you could not have found a solitary Doctor in Savannah who would not have hooted at the idea of contagion. Yellow Fever appeared here in 1827. There had not been a vessel of any

[7] Pertaining to marshes.

kind in Port for several months. This was before the days of Rail Roads and Steamers. Cotton was transported by river. Rivers dried up in the summer. Hence business was suspended entirely from the middle of July up to the beginning of October. No chance for any long low decked schooner to bring the disease from the West Indies, hidden under the peel of a banana or an orange, or lurking in the refreshing juice of a lime as one skillfully mixed it with the grateful Santa Cruz.

No one ever then doubted its local origin. Now I have frequently said, that Physicians should confine themselves to their own localities and give testimony as what they themselves have observed. Forty-four years have elapsed since that period. I say positively that in no instance has the Yellow Fever been of imported origin. I have reported in former times in the Journals, many cases where isolated cases have arrived from abroad and died here without any spread of the disease. I have seen three epidemics of Yellow Fever in Savannah in 1827, 1854, 1858. In intervening years I have seen Yellow fever, but not prevalent enough to be considered Epidemic. During the war, in 1862, when Savannah was closely blockaded I lost *eight* cases of Black Vomit, genuine Yellow Fever, with the boxwood-colored Liver.

In 1854, thousands left our plague stricken city carrying carpet bags, bandboxes, trunks, etc., etc. Many died after leaving, from the disease contracted in the city, scores had the genuine disease when away, yet never has there been known a solitary instance of propagation of the disease outside the limits of the City. Just after the Epidemic of 1854 I challenged the proofs of any such transmission of the disease.

Yellow fever is no more contagious than intermittant paludal fever, the germs of each are of telluric origin, e.g., Hutchinson Island, which you will recollect as immediately opposite to the city, is absolutely uninhabitable for the white race during the summer. After passing a hundred or so of yards, our high bluff is reached with its protecting row of high Brick Stores, and Savannah except on its very extreme suburbs is almost entirely free from Paludal fever. Congestive (the most malignant form of periodical fever) may be contracted in Hutchinson island, but cannot be propagated in the

City. Yellow Fever is strictly a city disease (not necessary for the city to be large), the disease contracted in the city has never in these parts been known to have been propagated in the country. Where, then, is the ground for the contagionist to stand upon? The long exemption of our Southern cities from epidemic Yellow fever in recent years had caused it to be but little thought about.

We know that it heretofore has prevailed in a regular cycle of years.

The causation of the disease is an intricate subject not susceptible of a very satisfactory solution.

I combat the contagiousness of Yellow fever because I do not believe in it and because the unfounded belief in it creates undue panic, needlessly obstructs commerce, interrupts all communication between sister cities, and cuts short the ordinary charities of social life. If a man has a fearful disease which exposes all who approach him to a similar contamination, will not the majority of mankind leave him to his fate?

I hope you will tolerate this rather long letter. Fever has been a subject of great excitement here. We have not had a solitary case or one approaching it in type, yet some persons have been constantly coming hither from Charleston. In 1838 & 1839 Yellow Fever prevailed extensively in Charleston & in 1839 in Augusta, Geo. The intercourse between those cities and this was free, and in those days no panic was created. But now official pickings follow contagious panics. I am sick of the rascality of the world.

July 13, 1872

Dr. Thomas T. Green,
Super. State Lunatic Asylum,
Milledgeville, Geo.

Your letter of the 4th came duly to hand. I cannot say that I have heard any reports to your disadvantage as to your management of the State Lunatic Asylum. I received some time since a pamphlet by one Nason or Vason relative to his treatment when in the Asylum, but I threw it aside as it simply proved that he was let out before he was cured. I recollect with pleasure that I used my personal influence with Governor Towns to have you retained in your position as Superintendent. I was opposed to the changes which had hitherto

been made by each incoming Governor, solely on political grounds. I advocated your claims because I thought you competent, and you displayed an enthusiasm in that Branch of our profession which gave a guarantee that you would do your work thoroughly. I had good opportunities for observing your conduct as Supt. from my frequent visits to Milledgeville whilst acting as Chairman of commissions for building the new Asylum. I always bore and I bear now my emphatic testimony as to your peculiar fitness for the situation, your excellent method and order, your judgement & strict economy in the management of the expenses, and the tact you displayed in your intercourse with your unfortunate patients, and the almost wonderful power over your patients, and your unflagging enthusiasm.

My confidence in you when I first advocated you to Governor Towns has been amply justified by what I have personally known of you since. Whatever cause may [lead] to the vacation of your position, it will be a public loss, for whatever qualifications your successor might bring, time alone could give him an experience like yours.

I have heard that the Asylum has been grossly neglected by the Scalawag Carpet-bag State Government which has just been so ignomiously kicked out of its usurped power, and that the means of the proper support of the Asylum had not been furnished, but I never heard any blame attached to you.

Nov. 8, 1872

Dr. E. F. Knoth, [?]
Griffin, Geo.

In reply to the main point of your letter, I have to state that in no way could I utalize the services of a young man in my office. No prescriptions are put in private offices in our city & I have a Bookkeeper familiar with my clients & with the city. Nor do I know of any opportunity which would suit you. I am no longer connected with the Savannah Medical College, except as one of its Trustees, but the present Faculty have my best wishes.

I retired voluntarily as a Professor two years since. I had delivered thirteen courses of Lectures on Theory & Practice, had spent several thousand dollars out of my pocket, & had exerted myself in every honorable manner for the success of the College. I feel proud that it

never lowered the Standard of Medical Education. The task has fallen into other & younger hands. . . . .

April 26, 1873

Dr. Elisha Harris of New York,
Sec. of the Am. Pub. H. Asso., to be at Cincinnatti, May,

Your communication of last fall informing me of my election as a member of the American Public Health Association was duly received. I delayed for a time to answer it, as I was constantly forgetting while at the Post office to obtain a Post office order to pay my initiation fee. Thus time rolled on, & I then determined to wait until I should be able to meet you in Cincinnatti & such was my intention until the last three days, when I found it to be out of the question for me to leave the city, & my visions of Cincinnatti & St. Louis have been dissipated into thin air. I regret the loss of my Cincinnatti visit more than that to St. Louis. The latter would be a trip merely of pleasure to renew old acquaintances, for although the record shows me as one of its Pioneers, I have long considered it[8] a failure in regard to the advancement of Medical Science or Medical Education.

The new Association aims at practical results which I think are quite obtainable. In the means of producing sanitary results our profession has always been in the front rank. An organized Association composed principally of Medical men from every section of the United States is very desirable. I should like much to be able to participate personally in the proceedings of the first meeting.

I wish, however, to keep up my connection with the Association as a Member, & accordingly enclose P. O. money order No. 28163 to your order for five dollars in payment of my initiation fee.

Nov. 14, 1875

Thomas J. Naylor (?),
Student of Medicine, Care of the Janitor,
Bellevue Medical College, New York.

I received with a great deal of pleasure your letter of the 7th inst. I am sure I have every reason to be proud of the praises bestowed on

[8] The American Medical Association.

me by my eminent medical Brethren of New York. You can now appreciate for your self the immense debt of gratitude I owe the eminent Dr. Thomas of Savannah for introducing me to the medical men of New York. I am gratified about the Flints (?), Father & son, because my intercourse with them has been more professional & not so personal as with many other medical men in New York. The tip top Doctors of New York are hard to beat on the score of liberality, hospitality, & keeness for Social enjoyment, while in their professional capacity they have their superiors no where. . . . .

Dr. Martin has returned. . . . . The doctor tells me that from a few words dropped by Billy Duncan, he infers that the Faculty of the Savannah Med College are getting a little tired. I always thought it was a little presumptuous in them to anticipate success, when the old Faculty with their own fine building and apparatus failed. The truth is there is not enough energy & talent (both of which are necessary) in the medical Profession here to ensure success. Every chair ought to be well filled. Compare Bellevue's Anatomy & Chemistry with that of Sav. Med. College. Enough said![9] . . . .

[9] For brief biographical notes on Arnold, see the usual collections of medical biography, e.g., W. B. Atkinson, *Physicians and Surgeons*, (1878); and the local histories of Savannah, e.g., C. C. Jones, et al., *History of Savannah*, (1890). See also the *Transactions of the American Medical Association*, XXIX, 615–618. For Arnold's connection with the formation of the A.M.A. consult N. L. Davis, *History of the American Medical Association to January, 1855*, (Phila., 1855). For the period of Arnold's greatest political activity see R. H. Shryock, *Georgia and the Union in 1850*, (1926).

BOOK REVIEWS

Standard Methods of the Division of Laboratories and Research of the New York State Department of Health. Edited by Augustus B. Wadsworth, M.D., Director. Pp. 704, with 74 illustrations. Cloth, $7.50. (*The Williams & Wilkins Company, Baltimore, 1927.*)

This book is unique in being the only comprehensive and detailed guide to practical public health laboratory methods and administration. With the exception of the Kahn precipitation test for syphilis, yet awaiting universal adoption, it brings together in well organized form precise details as to methods for carrying out almost every procedure used in diagnostic as well as in serum and vaccine laboratories. The sections on the production and standardization of sera and other biologic products are most complete and although, as the author states, there is still much empiricism in laboratory practice in this field, the methods include directions for the preparation of products of well recognized preventive or therapeutic value. Such information will be useful not only to those directly concerned, but also of interest to medical students and physicians who desire to gain knowledge of the more important immunological processes.

One of the most novel parts of the book which should prove helpful, especially to those concerned with the organization of public health laboratories, is that which deals with laboratory administration. This includes sample forms, directions for recording and reporting results of examinations, and for the distribution of laboratory preparations and outfits.

The work will serve as an excellent guide which the untrained or trained laboratory worker may follow or adapt to local conditions as the immediate situation may demand.

G. H. B.

Radio-Therapy in Relation to General Medicine. By Francis Hernaman Johnson, M.D. London, England. 203 pp. $1.75. (*Oxford University Press, 1926.*)

An excellent work for the student and practitioner asking for a general knowledge of radiotherapy, hardly intended primarily for the specialist. The physics of x-ray and radium are well presented and the relative value of the gamma ray of radium as compared with that of the present x-ray is correctly stated as far more effective, but we hardly share the hopes of the author that a penetration equal to radium will ever be developed in an x-ray tube. That most necessary precaution, protection to workers, is duly emphasized. The general nature of several of the important diseases amenable to ray therapy and the defensive reactions of the body are dwelt upon. The value of x-ray in cancer and sundry

benign diseases as treated by the author is elaborated; in this country we hardly anticipate such brilliant results. The chapter devoted to the therapy of Graves' disease and of the other ductless glands is especially helpful. The author's therapeutic experience being mostly with x-ray, we miss any authoritative exposition of radium therapy. He states that the reason radium therapy is not so highly developed as x-ray lies in the fact that only small amounts of radium are available in the British Isles; with a larger experience with more of the element he anticipates greatly improved results. In his clinic massive irradiation with four or five grams is at present out of the question. The choice of terms is not too technical and enables the reader to understand some of the possibilities, general principles and limitations of the subject.

W. N., Jr.

The Medical Department of the United States Army in the World War. Volume XI. Surgery, Part 1, General Surgery, Orthopedic Surgery and Neuro-Surgery. Prepared under the direction of Major General M. W. Ireland. 1324 pp. (*Government Printing Office, Washington, 1927.*)

Three sections are included in this volume: general surgery, orthopedic surgery and neuro-surgery. In the first are discussed the various weapons and missiles and the nature of the wounds caused by them.

The classification and care of the wounds are elaborated in great detail, from the application of first aid back through the various stations to the ultimate discharge of the patient from the army. The orthopedic section deals with organization, the use of splints and appliances in the treatment of defective feet, fractures, joint injuries and amputations. The section on neuro-surgery takes up organization, technique and the treatment of gun-shot wounds of the head, spine and peripheral nerves. Two chapters are devoted to motor and sensory disturbances in peripheral nerve lesions, while a third deals with experimental observations on peripheral nerve repair. The volume is extensively illustrated. There are 76 tables, 5 charts, 5 plates and 615 figures. The account given of outstanding advances and contributions to war surgery, débridement with primary or the delayed primary closure, the treatment of shock, fractures and the control of tetanus should prove of great value to the surgeon in civil practice, but more especially to those engaged in industrial work.

W. D. N.

A Manual of Pharmacology and its Applications to Therapeutics and Toxicology. By Torald Sollmann, Professor of Pharmacology and Materia Medica in the School of Medicine of Western Reserve University, Cleveland. Third Edition. 1184 pp. $7.50. (*W. B. Saunders Company, Philadelphia and London, 1926.*)

Sollmann's Manual of Pharmacology, since its first appearance, has been helpful, as the author intended, to the medical student and investigator as well

as to the practitioner. The present (third) edition contains descriptions of new drugs such as insulin, ethylene, and the parathyroid hormone, and most of the recent conceptions of chemotherapy, lead poisoning, and the autonomic nervous system. The bibliography has been extended and the book increased by 118 pages. The official preparations have been made to conform with the new (tenth) revision of the United States Pharmacopoeia. The author's thorough knowledge of his subject and his activity in the Council on Pharmacy and Chemistry of the American Medical Association and in the United States Pharmacopoeial Revision Committee has enabled him to write a textbook of really practical importance in medicine. The book will be especially appreciated by those who consult it frequently.

K. K. C.

Pathology and Treatment of the Inflammatory Diseases of the Nasal Accessory Sinuses. By PROFESSOR DR. M. HAJEK, Chief of the Laryngo-Rhino-Otological Clinic, University of Vienna. Translated and edited by Joseph D. Heitger, A.B., M.D., Louisville, Ky., and French K. Hansel, M.D., M.S., St. Louis, Missouri. Fifth Edition completely revised and enlarged, in two volumes. Pp. 702, with 186 illustrations and 3 plates. $17.00. (*C. V. Mosby Co., St. Louis, 1926.*)

The present edition is an excellent translation of Professor Hajek's valuable book, and is an exhaustive treaty on the anatomy, diseases, diagnosis and treatment of the nasal accessory sinuses. The style is good; the arguments logical. Case histories, as well as illustrations, are frequent and there is a valuable bibliography at the end of Volume II. The diseases of the antrum, ethmoid, frontal and sphenoid sinuses, along with their diagnosis and treatment, are dealt with in a very satisfactory way. There is also a valuable chapter on complications. The work is one that should be familiar to all rhinologists. The translators and publishers are to be congratulated.

E. N. B.

Pernicious Anemia. By BEAUMONT S. CORNELL. 311 pp. $4.00. (*Duke University Press, Durham, N. C.*)

At any time, but especially at this time of increased interest in pernicious anemia and its treatment, this book is tremendously valuable. His complete review of the literature, coupled with his own clinical and laboratory studies on the subject, have enabled Dr. Cornell to present a splendidly clear picture of pernicious anemia. He traces the evolution of the conception of the disease from Combe's first description of it in 1822, through the writings of Addison, Hunter, Cohnheim, Ehrlich and others, to the modern era established by Whipple, Howard, Gibson, Minot and Murphy. He evaluates the various classifications, hypotheses and ideas of the Continental, English and American schools, winnowing the chaff from the wheat, and analyzes our present position, clearly pointing

out the facts we know and the phases of which we are ignorant. Every student should familiarize himself with the historical background of this disease and the efforts which have been made to find its cause, in order to appreciate its present status. Anyone who has read Dr. Cornell's survey of the etiological studies in pernicious anemia will become a skeptic of any future theory in regard to it and not form an opinion based on personal conviction like that in politics, to quote a review of another book on this subject. Dr. Cornell summarizes the present conception of pernicious anemia as "a superstructure of blood system and nervous system changes superimposed upon an unknown foundation of which achlorhydria is the almost constant and only obvious expression." The various etiological factors, such as bacterial infection, intestinal intoxication and constitutional diathesis, which have been brought to the bar, have received the Scotch verdict of "not proven."

Dr. Cornell's descriptions of the numerous clinical manifestations of the disease are vividly graphic and hold the attention of any student of medicine even if he, like the reviewer, practices a specialty in which this disease is not encountered. The accounts of several patients who illustrate different phases of the disease are absorbing. The symptoms which are caused by changes in the various systems give one an orderly picture of the disease. His description of the changes in the blood is most instructive and is presented so interestingly that even a hurried reading impresses it on the memory.

Among the many valuable features are a complete discussion of the differential diagnosis, the pathological data, the tables and charts and the interesting information on the geographical distribution of the disease with its high incidence in Ontario. The successful "liver" therapy of Minot and Murphy is discussed in detail together with appropriate diets.

As Dr. Cornell says, the more intimate one's knowledge of pernicious anemia becomes, the fewer will be the diagnostic difficulties encountered. Of course no one can fully appreciate this disease without studying patients, but this book will provide the sailing charts to which Osler referred in his aphorism, "To study the phenomena of disease without books is to sail an uncharted sea, while to study books without patients is not to go to sea at all." As a matter of fact, the splendid results of "liver" therapy have made active cases of pernicious anemia exceedingly rare and Dr. Cornell had to travel extensively to find clinical material for his studies.

One great asset of this book, so unfortunately rare in modern medical literature, is that it is well written and readable. Dr. Cornell is a Fellow of Duke University and, therefore, his book on the disease of which Mr. Duke died is of sentimental as well as practical import. Dr. Campbell P. Howard, a pioneer in the present treatment of pernicious anemia, has supplied a felicitous introduction.

W. C. D.

A Guide for Diabetics. By CAMPBELL and PORTER. 256 pp. $2.50. (*The Williams & Wilkins Company, Baltimore, Md.*)

This is another of many recent diabetic manual publications designed to explain to the patient certain facts about diabetes and its dietetic control, and thus enable more intelligent coöperation with the physician. The first one hundred pages deal entirely with the disease, its treatment, insulin therapy, its dangers, etc. as a guide for the patient, with blank pages interleaved with each printed page for the patient's notations, an excellent idea.

The rest of the book is devoted to dietary material with a view to instructing the patient to work out his own diets. There are recipes, food equivalents, food substitutions as well as food analyses. Perhaps the material is a little above the intelligence of the average clinical patient, but were it possible to educate them through such a manual, a splendid variety could be initiated into the monotonous diabetic diets. It is an excellent book and one to be recommended to patients who are intellectually and financially able to follow its suggestions.

F. E. B.

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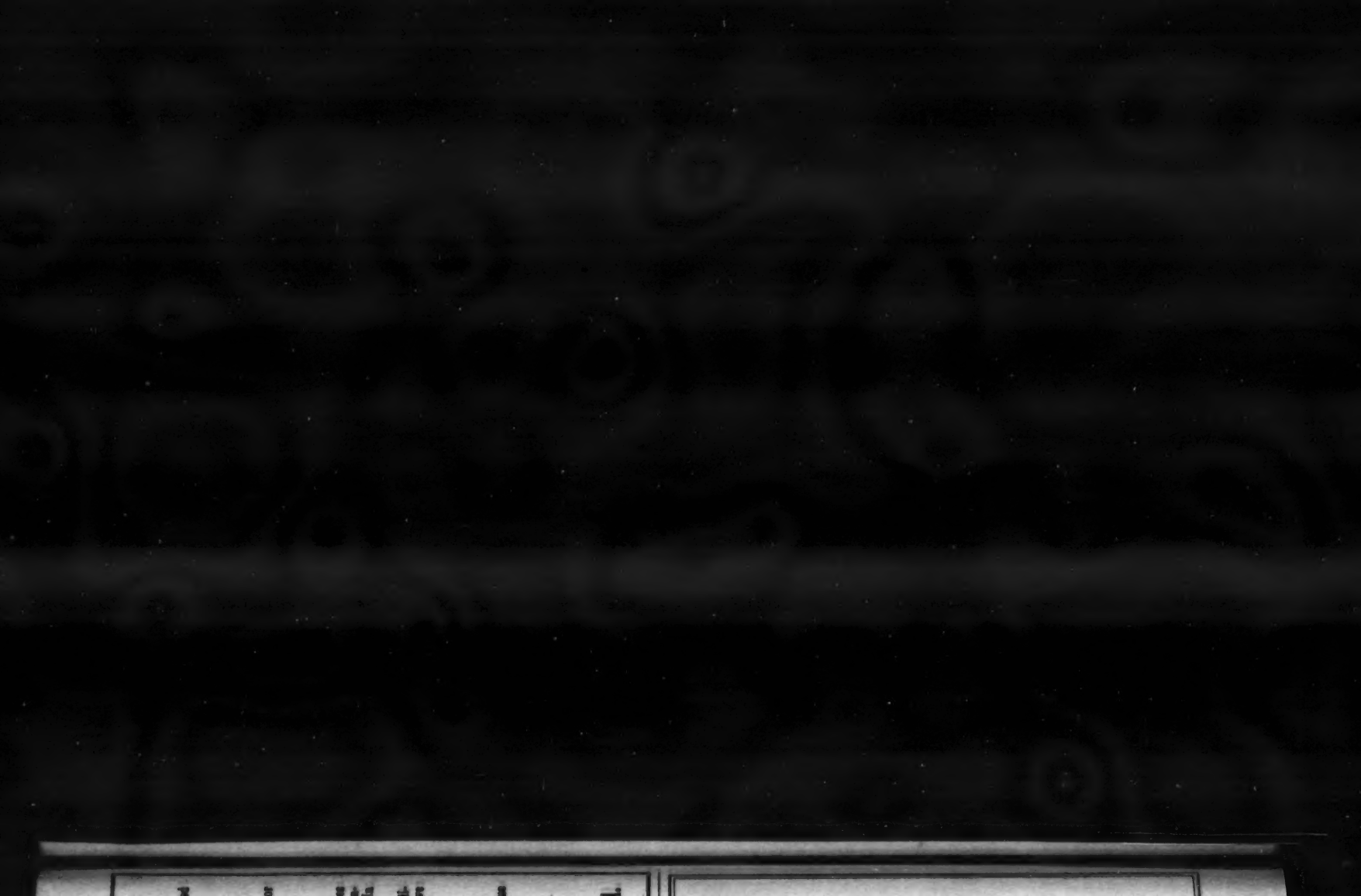
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